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Tina Powers
VERTEX PHARMACEUTICALS INC.
130 Waverly Street
Cambridge, MA 02139-4242

EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/008,277	SALITURO ET AL.	
	Examiner	Art Unit	
	Deepak R Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *93002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-12 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation of compounds of Formula I and the pharmaceutically acceptable salts thereof, does not reasonably provide enablement for 'pharmaceutically acceptable derivative or prodrug thereof'. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The instant claim recites "A compound ... or pharmaceutically acceptable **derivative** or **prodrug** thereof" wherein there is insufficient description in the specification regarding the types of 'derivatives' and 'prodrugs' intended by the recitation. The recitation "pharmaceutically acceptable derivative or prodrug" is

explained in the specification at page 15 as 'salt, ester, salt of an ester or other derivative..... inhibitorily active metabolite or residue thereof'. However, the specification does not provide what "other derivatives" are intended by this recitation.

In general compounds 'that increase the bioavailability of a compounds' are known as prodrugs. It is also known that many examples of "prodrugs" include 'esters' that may hydrolyzed *in vivo* to the acids. However, the definition of various substituent groups in formula (I) already include such groups, i.e., acids as well as esters. The specification does not provide what other 'compounds' of the invention are intended to be prodrugs. The generic formulae of the claims already include both esters and the corresponding free acid forms, see e.g., see the term " -C(O)-X-R_2 wherein X is O and R_2 is H, alkyl, etc. " There is no disclosure regarding any other esters that are capable of providing compounds of the invention. Similarly, the term "metabolite" is not sufficiently described. A metabolite is any compound which is pharmaceutically active *in vivo* when it undergoes 'metabolic' process and the specification does not provide any disclosure of what these compounds might be that *in vivo* transform in to the instantly claimed compounds. The specification does not provide what other 'compounds' of the invention are intended to be prodrugs or metabolites. Since both esters and acids are already included in the claimed compounds, it is not clear whether compounds bearing these groups are excluded from being a potential "prodrug" or "metabolite". If compounds bearing these groups (i.e., ester, etc.), which are likely to undergo *in vivo* transformation, are excluded then what is included in the definition of 'prodrug' and where on the structural formula (I) are these groups placed; the specification does not provide any direction to one of ordinary skill in the art.

Claims 4-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating rheumatoid arthritis, does not reasonably provide enablement for treating of all other diseases of the instant claims; or preventing the diseases of the instant claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to "a method treating or preventing inflammatory diseases, autoimmune disease, proliferative disorder, infectious diseases, ...". First, the instant claims cover 'diseases' that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The use disclosed in the specification is as JNK inhibitors, useful to treat a laundry list of diseases, which include proliferative disorders, inflammatory diseases, autoimmune diseases, neurodegenerative diseases, allergies, etc. Test assays and procedures are provided in the specification in Examples 3-5 related to JNK inhibition, however, none of the instantly claimed

compounds are tested for the activity. Further, there is nothing in the disclosure regarding how this *in vitro* test procedure correlates to the treatment of the diverse disorders of the instant claims. The disorders encompassed by the instant claims include proliferative disorders, inflammatory diseases, neurodegenerative diseases, etc., some of which have been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

Further, the instant claims recite 'treating or preventing various diseases', and there is no disclosure regarding how all these assorted types diseases are treated using the single class of compounds. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area, as evidenced by the wide range of results obtained for the tested compounds. It is inconceivable as to how the claimed compounds can treat the laundry list of diseases embraced by the claims having diverse mechanisms. Applicant has not provided sufficient evidence based on the biological activity of the compounds, how all types of diseases of the instant claims are treated or the severity of the diseases are lessened.

A 'proliferative disorder' is anything that causes abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of

structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, polyps, etc. No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "silver bullet" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163 USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. In reference to cancer treatment using protein tyrosine kinase inhibitors, Traxler (Exp. Opin. Ther. Patents, 1997) stated that "pharmacological properties such as stability in biological media, bioavailability, metabolism or formulability are significant hurdles" see page 585, col. 2, lines 33-36.

It is inconceivable as to how the claimed compounds can treat all types of infectious diseases. There is no known common therapeutic mechanism for all types of infectious diseases generally. For example, there are more than 400 distinct viruses that infect humans producing a wide range of diseases. Another online reference states, "Bacterial infections are caused by the presence and growth of microorganisms that damage host tissue. The extent of infection is generally determined by how many

organisms are present and the toxins they release." see http://www.lef.org/protocols/prtcl-018.shtml. Cecil Textbook of Medicine states that "for many viral infections, no specific therapy exists. Proper use of antivirals requires specific viral diagnosis" (see the enclosed article, page 1742).

The claims recite the use of the instantly claimed compounds in treating 'angiogenic disorder'. Angiogenesis is the process of vascularization of a tissue involving the development of new capillary blood vessels and therefore, is not seen as being a disease or disorder, but as an absolutely essential body process. Thus, there is no enablement for treating something which is not itself a problem and is indeed essential for life.

Also, there is no common mechanism by which all inflammatory conditions arise. The mediators include bradykinin, serotonin, histamine, assorted leukotrienes, cytokines, etc. Accordingly, treatments for these diseases are normally tailored to the particular type of inflammation or infection present and there is no "magic bullet" against the plethora of diseases encompassed by the instant claims. Enablement for the scope of "inflammation" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of

circulating neurophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages, which have stuck tightly together, typically to wall something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. Otitis media is an inflammation of the lining of the middle ear and is commonly caused by Streptococcus pneumoniae and Haemophilus influenzae. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

Further, the list of the diseases includes neurodegenerative diseases (see specification page 19) which covers diverse disorders such as Alzheimer's disease, dementia, hereditary cerebellar ataxias, paraplegias, syringomyelia, phakomatoses, and much more. In fact, Layzer, Cecil Textbook of Medicine (article enclosed), states that "some degenerative diseases are difficult to classify because they involve multiple anatomic locations" (see page 2050). For example, Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively with chemotherapeutic agents. See e.g., the Cecil Textbook of Medicine, 20th edition (1996), Vol. 2, wherein it is stated that "[t]here is no cure for Alzheimer's disease, and no drug tried so far can alter the progress of the disease." (pg. 1994).

The Merck Manual of Diagnosis and Therapy (1999) provides that 'the initial lung injury in adult respiratory distress syndrome (ARDS) is poorly understood'; "Many approaches to the prevention and management of ARDS have been unsuccessful or inconclusive"; and "Several approaches show promise but need further study". Elgert (Immunology, 1996) indicate factors that effect autoimmune diseases include dysfunction in cytokine production, thymic defects, genetic factors, hormonal factors, etc. The author further comments regarding insulin dependent diabetes mellitus that "The only diabetes treatment is replacement therapy through insulin injections" (page 323); "Systemic lupus erythematosus (SLE) is an inflammatory connective tissue disease of unknown cause" (page 324).

The instant claims include treatment of inflammatory bowel disease including Crohn's disease and ulcerative colitis which have been proven very difficult to treat because 'there is no known cause' (see The Merck Manual). Bremner et al. (Expert

Opin. Pharmacother. 2002) provide that "New therapies that affect immunomodulation offer the possibility of disease control in those unresponsive to conventional therapy and may reduce the need for further surgery. However, these treatments remain to be fully evaluated" (see page 820). Singh et al. (British Journal of Surgery, 2001) provide that 'the etiology and pathogenesis of inflammatory bowel diseases are incompletely understood' (see page 1558). Robinson (Eur. J. Surg. 1998) indicates that "Despite the growing list of medications and formulations prompted for the treatment of IBD, no single drug or recognized combination has yet been confirmed as dependably clinically effective"; "All physicians who care for UC and CD patients enthusiastically await more optimal regimens for these challenging disorders" (see page 90). This is indicative of the unpredictability related to the treatment of inflammatory bowel diseases.

Further, the list of the diseases includes multiple sclerosis which has traditionally been very difficult or impossible to treat effectively with chemotherapeutic agents. See e.g., Casanova et al. (PubMed Abstract enclosed) state that "Multiple Sclerosis (MS) is a disorder in which the pathogenesis is not clearly understood", see the abstract.

The instant claims also recite 'a method of treating or preventing .... conditions associated with proinflammatory cytokines' which covers any disease or disorder related to body or mind, and thereby does not limit to the specific diseases which are disclosed in the specification. The instant claim language covers diseases that are very difficult to treat, e.g., cancer, multiple sclerosis, etc. and diseases that are yet to be discovered, for which there is no enablement provided. The state of the art also presents the difficulties encountered in the method of controlling the extracellular release of inflammatory cytokines, see Holzheimer (PubMed Abstract enclosed), "The effect of antibiotics on the

release of endotoxin and inflammatory parameters, e.g., cytokines, **remains to be clarified** despite a growing body of in-vitro studies, animal studies and a few clinical studies". Also, see van Deventer (PubMed Abstract enclosed), "no human cytokine deficiency syndromes are known, and **it remains uncertain** whether genetically determined differences in the production rate of pro-inflammatory cytokines alter the outcome of sepsis". Another state of the art reference, Green et al. (PubMed Abstract enclosed) regarding the effect of TNF-α on the progression of diabetes, states that "the mechanism by which TNF-alpha exerts these differential outcomes is unknown". Rasmussen (PubMed Abstract enclosed) regarding cytokine actions on the thyroid gland, proclaims that "A better understanding of pathogenic mechanisms is crucial for an appropriate and effective management of AITD".

Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed therapeutic effect on these assorted diseases solely based on the *in vitro* inhibitory activity disclosed for the compounds.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Traxler, in a recent article (Exp.

Opin. Ther. Patents, 1997) stated that "The concept of the inhibition of growth factor receptor-mediated signal transduction via inhibition of its protein tyrosine kinase is a novel, **not yet proven** clinical approach to the regulation of cell proliferation.", see page 585, col. 1. Therefore, the state of the art provides the need of undue experimentation for the instantly claimed therapeutic benefits.

The instant claims recite 'a method of treating or **preventing**' and therefore, the instant claim language embraces disorders not only for the treatment, but also for "prevention" which is not remotely enabled. Based on the inhibitory activity, the instant compounds are disclosed to be useful in the "prevention" of proliferative diseases, neurodegenerative disorders, for which applicants provide no competent evidence. "To prevent" actually means *to anticipate* or *counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the '**preventive**' effect. It is inconceivable how the *in vitro* test procedures provided in the specification convey to one of ordinary skill in the art a correlation to the 'treating or preventing' of the various disorders of the instant claims. Further, there is no evidence on record which demonstrates that the *in-vitro* screening test relied upon is recognized in the art as being reasonably predictive of success in any of the contemplated areas of 'preventing'. Such a reasonable correlation is necessary to demonstrate such utilities. See *Ex parte Stevens*, 16 USPQ 2d 1379 (BPAI 1990); *Ex parte Busse et al.*, 1 USPQ 2d 1908 (BPAI 1986) (the evidence must be accepted as "showing" such utility, and not "warranting further study").

(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Bell et al. (J. Het. Chem. 1983). The instant claims read on reference disclosed compound, see compound 14 in page 42. The reference discloses the compound in the presence of a solvent and therefore, teaches a composition comprising the compound and a solvent. The preamble and intended use recitation in the composition claim are not given patentable weight.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Tominaga et al. (J. Het. Chem. 1991). The instant claims read on reference disclosed compound, see compounds 5i and 5j in page 1040. The reference discloses the compound in the presence of a solvent and therefore, teaches a composition comprising the compound and a solvent. The preamble and intended use recitation in the composition claim are not given patentable weight.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 3-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Machon et al., Chem. Abstract 97:84779. The reference teaches compounds of 1,2,3,6-tetrahydro-2,6-dioxo-pyrimidine compounds, see the compounds disclosed in the

abstract. The compounds have carboxylate group attached to the 4-position and a substituted amino group at the 5-position of the pyrimidine. The instantly claimed compounds reverse the positions of the reference compounds i.e., a carboxyl group is at the 4-position and a $-Y-R_1$ wherein Y is NH is at the 5-position. The reference compounds are taught to possess anti-inflammatory and analgesic therapeutic activity, see the abstract. Since the instantly claimed compounds differ only by the positions of the substituents, they are positional isomers of the reference compounds. It would have been obvious to one having ordinary skill in the art at the time of the invention to prepare the instantly claimed compounds because they are isomers of the reference compounds. One having ordinary skill in the art would have been motivated to prepare the instantly claimed compounds because such structurally isomeric compounds are suggestive of one another and would be expected to share similar properties and therefore, the same use as taught for the reference compounds. It has been held that a compound which is isomeric with a compound of prior art is prima facie obvious absent unexpected results. *In re Finley*, 81 USPQ 383 (CCPA 1949); *In re Norris*, 84 USPQ 458 (CCPA 1950). *In re Dillon*, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990).

Receipt is acknowledged of the Information Disclosure Statement filed on September 30, 2002 and a copy is enclosed herewith.

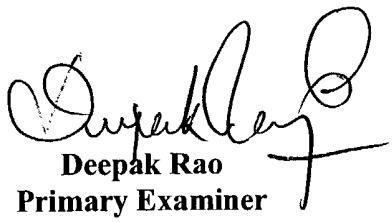
Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Deepak Rao
Primary Examiner
Art Unit 1624

June 24, 2004